Claims

1. A fusion protein comprising an interferon-alpha (IFN-α) molecule joined at its C terminal end through a peptide linker to an N terminal end of an immunoglobulin heavy chain comprising a hinge, C_H2, and C_H3 domain, wherein the linker has a sequence chosen from Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (GS10; SEQ ID NO:28), Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (GS15; SEQ ID NO:29), and Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (GS20; SEQ ID NO:30).

2. The fusion protein of claim 1, wherein the IFN-α is IFN-α2b.

3. The fusion protein of claim 1, wherein the IFN-α is a consensus IFN.

4. The fusion protein of claim 1, wherein the immunoglobulin heavy chain is a human Fcγ1 heavy chain.

5. The fusion protein of claim 1, wherein the immunoglobulin heavy chain has an amino acid sequence provided by SEQ ID NO:2.

6. The fusion protein of claim 1, wherein the IFN-α is IFN-α2b and the immunoglobulin heavy chain is a human Fcγ1 heavy chain.

7. The fusion protein of claim 1, wherein the linker has a sequence Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (GS10; SEQ ID NO:28).

8. The fusion protein of claim 1, wherein the linker has a sequence Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (GS15; SEQ ID NO:29).

9. The fusion protein of claim 1, wherein the linker has a sequence Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (GS20; SEQ ID NO:30).

10. The fusion protein of claim 1, wherein the fusion protein is a disulfide-linked homodimer.

11. A fusion protein comprising an interferon-alpha 2b (IFN-α2b) molecule joined at its C terminal end through a peptide linker to an N terminal end of a human Fcγ1 heavy chain comprising a hinge, C_H2, and C_H3 domain, wherein the linker has a sequence Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (GS15; SEQ ID NO:29).

12. The fusion protein of claim 1, wherein the fusion protein is a disulfide-linked homodimer.

13. A method for systemic delivery of interferon-alpha (IFN-α), comprising:

administering an effective amount of an aerosol of a fusion protein of claim 1 to lung such that a central lung zone/peripheral lung zone deposition ratio (C/P ratio) is at least 0.7.

14. The method of claim 13, wherein the C/P ratio is at least 1.0.

15. The method of claim 13, wherein the C/P ratio is at least 1.5.

16. The method of claim 13, wherein the C/P ratio is at least 2.0.

17. The method of claim 13, wherein the fusion protein is a disulfide-linked homodimer.

18. A method for systemic delivery of interferon-alpha 2b (IFN-α2b), comprising:

administering an effective amount of an aerosol of a fusion protein of claim 11 to lung such that a central lung zone/peripheral lung zone deposition ratio (C/P ratio) is at least 0.7.

19. The method of claim 18, wherein the C/P ratio is at least 1.0.

20. The method of claim 18, wherein the C/P ratio is at least 1.5.

21. The method of claim 18, wherein the C/P ratio is at least 2.0.

22. The method of claim 18, wherein the fusion protein is a disulfide-linked homodimer.

23. A method for systemic delivery of interferon-alpha (IFN-α), comprising:
administering an effective amount of an aerosol of a fusion protein of claim 1 to lung, wherein particles in the aerosol have a mass median aerodynamic diameter (MMAD) of at least 3 micrometers (μm).

24. The method of claim 23, wherein the MMAD of the particles is between 3 μm and about 8 μm.

25. The method of claim 23, wherein the MMAD of the particles is greater than 4 μm.

26. The method of claim 23, wherein a majority of the particles are non-respirable.

27. The method of claim 23, wherein the fusion protein is a disulfide-linked homodimer.

28. A method for systemic delivery of interferon-alpha 2b (IFN-α2b), comprising:
administering an effective amount of an aerosol of a fusion protein of claim 11 to lung, wherein particles in the aerosol have a mass median aerodynamic diameter (MMAD) of at least 3 micrometers (μm).

29. The method of claim 28, wherein the MMAD of the particles is between 3 μm and about 8 μm.

30. The method of claim 28, wherein the MMAD of the particles is greater than 4 μm.

31. The method of claim 28, wherein a majority of the particles are non-respirable.

32. The method of claim 28, wherein the fusion protein is a disulfide-linked homodimer.

33. An aerosol delivery system, comprising a container, an aerosol generator connected to

the container, and a fusion protein of claim 1 disposed within the container, wherein the aerosol generator is constructed and arranged to generate an aerosol of the fusion protein having particles with a MMAD of at least 3 μm.

34. The aerosol delivery system of claim 33, wherein the MMAD of the particles is greater than 4 μm.

35. The aerosol delivery system of claim 33, wherein a majority of the particles are non-respirable.

36. The aerosol delivery system of claim 33, wherein the aerosol generator comprises a vibrational element in fluid connection with a solution containing the fusion protein.

37. The aerosol delivery system of claim 33, wherein the aerosol generator is a nebulizer.

38. The aerosol delivery system of claim 33, wherein the aerosol generator is a mechanical pump.

39. The aerosol delivery system of claim 33, wherein the container is a pressurized container.

40. An aerosol delivery system, comprising a container, an aerosol generator connected to the container, and a fusion protein of claim 11 disposed within the container, wherein the aerosol generator is constructed and arranged to generate an aerosol of the fusion protein having particles with a MMAD of at least 3 μm.

41. The aerosol delivery system of claim 40, wherein the MMAD of the particles is greater than 4 μm.

42. The aerosol delivery system of claim 40, wherein a majority of the particles are non-respirable.

43. The aerosol delivery system of claim 40, wherein the aerosol generator comprises a vibrational element in fluid connection with a solution containing the fusion protein.

44. The aerosol delivery system of claim 40, wherein the aerosol generator is a nebulizer.

45. The aerosol delivery system of claim 40, wherein the aerosol generator is a mechanical pump.

46. The aerosol delivery system of claim 40, wherein the container is a pressurized container.

47. A method of treating an interferon-alpha (IFN-α)-sensitive disease in a subject, comprising

administering to a subject having an IFN-α-sensitive disease an aerosol of the fusion protein of claim 1, in an effective amount to treat the IFN-α-sensitive disease.

48. The method of claim 47, wherein the IFN-α-sensitive disease is chosen from hairy cell leukemia, AIDS-related Kaposi's sarcoma, chronic phase Philadelphia chromosome-positive chronic myelogenous leukemia, malignant melanoma, follicular lymphoma, condylomata acuminata, chronic hepatitis C, and chronic hepatitis B.

49. A method of treating an interferon-alpha 2b (IFN-α2b)-sensitive disease in a subject, comprising

administering to a subject having an IFN-α2b-sensitive disease an aerosol of the fusion protein of claim 11, in an effective amount to treat the IFN-α2b-sensitive disease.

50. The method of claim 49, wherein the IFN-α2b-sensitive disease is chosen from hairy cell leukemia, malignant melanoma, follicular lymphoma, condylomata acuminata, AIDS-related Kaposi's sarcoma, chronic hepatitis C, and chronic hepatitis B.